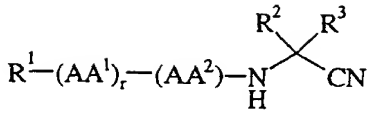
CLAIMS

1. A compound of formula (I):



(I)

wherein

r is 0 or 1;

R^1 is hydrogen, optionally substituted benzyl where said optional substituents are chosen from one or more of C_{1-6}alkyl, halo, trifluoromethyl, hydroxy, trifluoromethoxy, cyano, C_{1-6}alkoxy, C_{1-6}alkanoyl, C_{1-6}alkanoyloxy, amino, C_{1-6}alkylamino, *N,N*-(C_{1-6}alkyl)$_2$amino, C_{1-6}alkanoylamino, nitro, carboxy, carbamoyl, *N*-(C_{1-6}alkyl)carbamoyl, *N,N*-(C_{1-6}alkyl)$_2$carbamoyl, C_{1-6}alkoxycarbonyl, mercapto, C_{1-6}alkylsulphanyl, C_{1-6}alkylsulphinyl, C_{1-6}alkylsulphonyl, sulphamoyl, *N*-(C_{1-6}alkyl)sulphamoyl and *N,N*-(C_{1-6}alkyl)$_2$sulphamoyl, or R^1 is a group of formula (II):

(II)

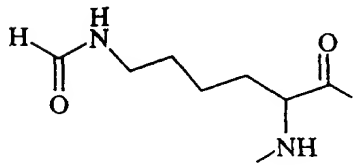
wherein R^5 is C_{1-6}alkyl (optionally substituted with an optionally substituted phenyl, an optionally substituted 5 or 6 membered heteroaryl ring, optionally substituted phenoxy, optionally substituted phenylsulphonyl, optionally substituted C_{3-12}cycloalkyl or Het), C_{1-6}alkoxy, optionally substituted phenyl, optionally substituted naphthyl, optionally substituted 5 or 6 membered heteroaryl ring, optionally substituted C_{3-12}cycloalkyl, Het or optionally substituted phenylC_{1-6}alkoxy; where said optional substituents are chosen from one or more of C_{1-6}alkyl, halo, trifluoromethyl, hydroxy, trifluoromethoxy, cyano, C_{1-6}alkoxy, C_{1-6}alkanoyl, C_{1-6}alkanoyloxy, amino, C_{1-6}alkylamino, *N,N*-(C_{1-6}alkyl)$_2$amino, C_{1-6}alkanoylamino, nitro, carboxy, carbamoyl, *N*-(C_{1-6}alkyl)carbamoyl, *N,N*-(C_{1-6}alkyl)$_2$carbamoyl, C_{1-6}alkoxycarbonyl, mercapto,

C_{1-6}alkylsulphanyl, C_{1-6}alkylsulphinyl, C_{1-6}alkylsulphonyl, sulphamoyl, *N*-(C_{1-6}alkyl)sulphamoyl and *N,N*-(C_{1-6}alkyl)$_2$sulphamoyl;

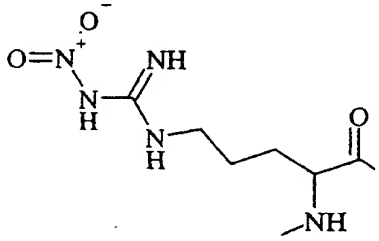
$\mathbf{R^2}$ is H, C_{1-6}alkyl [optionally substituted with one or more of hydroxy, C_{1-6}alkylsulphanyl, C_{1-6}alkylsulphinyl, C_{1-6}alkylsulphonyl, R^4, R^4C_{1-6}alkylsulphanyl, R^4C_{1-6}alkylsulphinyl, R^4C_{1-6}alkylsulphonyl], or R^2 is C_{1-6}alkoxy [optionally substituted with one or more of C_{2-6}alkenyl, C_{2-6}alkynyl, R^4, R^4C_{2-6}alkenyl, R^4C_{2-6}alkynyl, Het and trifluoromethyl], or R^2 is C_{2-6}alkenyl, C_{2-6}alkynyl, C_{1-6}alkoxycarbonyl, carbamoyl, *N*-(C_{1-6}alkyl)carbamoyl, *N,N*-(C_{1-6}alkyl)$_2$carbamoyl, R^4, R^4S, R^4C_{1-6}alkylsulphanyl, *N*-(R^4C_{1-6}alkyl)carbamoyl, *N*-(HetC_{1-6}alkyl)carbamoyl, C_{1-6}alkanoylamino, C_{1-6}alkylsulphanyl, C_{1-6}alkylsulphinyl or C_{1-6}alkylsulphonyl; $\mathbf{R^4}$ is an optionally substituted phenyl or an optionally substituted 5 or 6 membered heteroaryl ring containing a maximum of four heteroatoms, said optional substituents being chosen from one or more of C_{1-6}alkyl, halo, trifluoromethyl, hydroxy, trifluoromethoxy, cyano, C_{1-6}alkoxy, C_{1-6}alkanoyl, C_{1-6}alkanoyloxy, amino, C_{1-6}alkylamino, *N,N*-(C_{1-6}alkyl)$_2$amino, C_{1-6}alkanoylamino, nitro, carboxy, carbamoyl, *N*-(C_{1-6}alkyl)carbamoyl, *N,N*-(C_{1-6}alkyl)$_2$carbamoyl, C_{1-6}alkoxycarbonyl, mercapto, C_{1-6}alkylsulphanyl, C_{1-6}alkylsulphinyl, C_{1-6}alkylsulphonyl, sulphamoyl, *N*-(C_{1-6}alkyl)sulphamoyl and *N,N*-(C_{1-6}alkyl)$_2$sulphamoyl;

$\mathbf{R^3}$ is H or C_{1-6}alkyl;

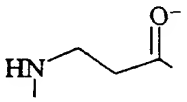
($\mathbf{AA^1}$) and ($\mathbf{AA^2}$) are independently chosen from Ala, Arg, Cys, Gly, His, Ile, Leu, Lys, Met, Phe, Ser, Thr, Trp, Tyr, Val,



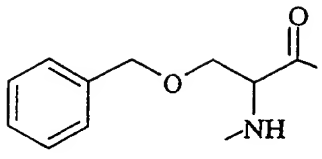
Lys(CHO),



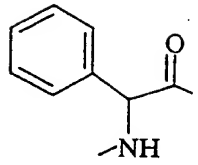
Arg(NO_2),



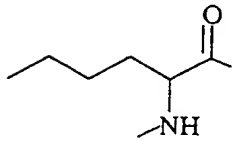
β-Ala,



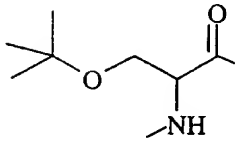
Ser(Bzl),



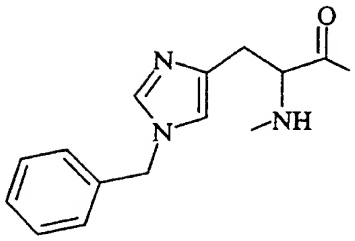
Ph-Gly,



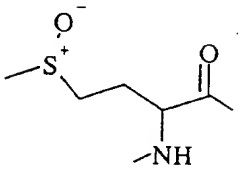
Nle,



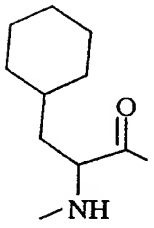
Ser(O^{t}Bu),



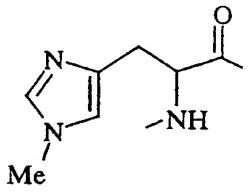
His(Bzl),



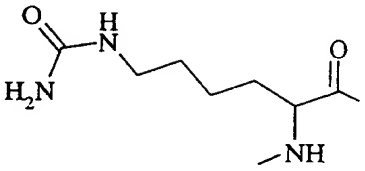
Met(O),



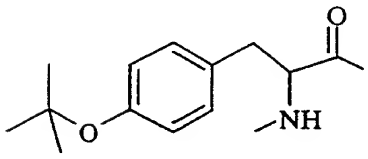
Cha,



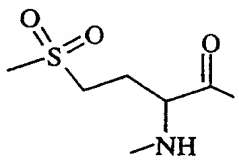
His(Me),



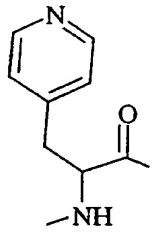
Cit,



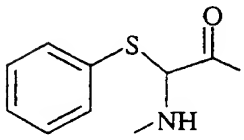
Tyr(^{t}Bu),



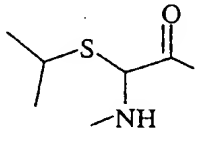
Met(O_2),



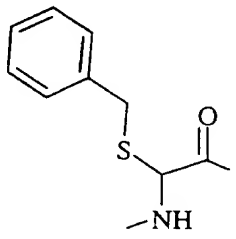
Pyr-Ala



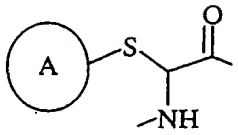
Phe(S),



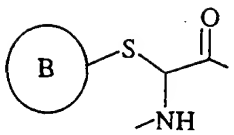
Leu(S),



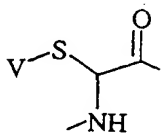
Phe(CH_2S),



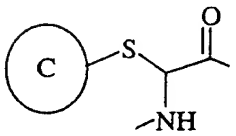
Cy(S)-Gly,



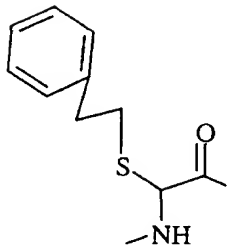
Hetar(S)-Gly,



alk(S)-Gly or



Het(S)-Gly, and



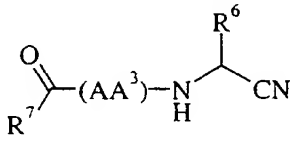
Phe(CH_2CH_2)S;

wherein Ring A is C_{3-12}cycloalkyl; Ring B is a 5 or 6 membered heteroaryl ring; Ring C is Het; V is C_{1-6}alkyl excluding isopropyl; the nitrogen of the amino acid may optionally be alkylated with C_{1-6}alkyl; the phenyl group of Phe(S) and Rings A and B are optionally substituted with one or more of C_{1-6}alkyl, halo, trifluoromethyl, hydroxy, trifluoromethoxy, cyano, C_{1-6}alkoxy, C_{1-6}alkanoyl, C_{1-6}alkanoyloxy, amino, C_{1-6}alkylamino, *N,N*-(C_{1-6}alkyl)$_2$amino, C_{1-6}alkanoylamino, nitro, carboxy, carbamoyl, *N*-(C_{1-6}alkyl)carbamoyl, *N,N*-(C_{1-6}alkyl)$_2$carbamoyl, C_{1-6}alkoxycarbonyl, mercapto, C_{1-6}alkylsulphanyl, C_{1-6}alkylsulphinyl, C_{1-6}alkylsulphonyl, sulphamoyl, *N*-(C_{1-6}alkyl)sulphamoyl or *N,N*-(C_{1-6}alkyl)$_2$sulphamoyl; the phenyl group of Phe(S) may be fused to another phenyl group to form a naphthyl group; the sulphur moiety in the ∝-position of the amino acid (AA^3) may be optionally oxidised to form an -S(O)$_2$- or -S(O)- moiety; and

Het is a fully saturated monocyclic 5 - 8 membered heterocyclic ring, with up to 4 ring heteroatoms;

or a pharmaceutically acceptable salt thereof.

2. A compound as claimed in claim 1 having the formula (**Ia**):



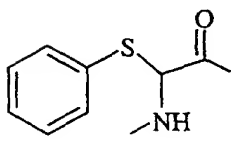
(Ia)

wherein:

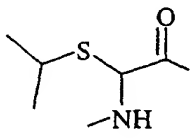
$\mathbf{R^7}$ is optionally substituted benzyl, optionally substituted phenoxymethyl, optionally substituted phenylsulphonylmethyl, optionally substituted benzyloxy, optionally substituted naphthyl, optionally substituted phenyl or t-butoxy where said optional substituents are chosen from one or more of C_{1-6}alkyl, halo, trifluoromethyl, hydroxy, trifluoromethoxy, cyano, C_{1-6}alkoxy, C_{1-6}alkanoyl, C_{1-6}alkanoyloxy, amino, C_{1-6}alkylamino, *N,N*-(C_{1-6}alkyl)$_2$amino, C_{1-6}alkanoylamino, nitro, carboxy, carbamoyl, *N*-(C_{1-6}alkyl)carbamoyl, *N,N*-(C_{1-6}alkyl)$_2$carbamoyl, C_{1-6}alkoxycarbonyl, mercapto, C_{1-6}alkylsulphanyl, C_{1-6}alkylsulphinyl, C_{1-6}alkylsulphonyl, sulphamoyl, *N*-(C_{1-6}alkyl)sulphamoyl and *N,N*-(C_{1-6}alkyl)$_2$sulphamoyl;

$\mathbf{R^6}$ is hydrogen, optionally substituted phenyl or optionally substituted 5 or 6 membered heteroaryl ring containing a maximum of four heteroatoms; said optional substituents being chosen from one or more of C_{1-6}alkyl, halo, trifluoromethyl, hydroxy, trifluoromethoxy, cyano, C_{1-6}alkoxy, C_{1-6}alkanoyl, C_{1-6}alkanoyloxy, amino, C_{1-6}alkylamino, *N,N*-(C_{1-6}alkyl)$_2$amino, C_{1-6}alkanoylamino, nitro, carboxy, carbamoyl, *N*-(C_{1-6}alkyl)carbamoyl, *N,N*-(C_{1-6}alkyl)$_2$carbamoyl, C_{1-6}alkoxycarbonyl, mercapto, C_{1-6}alkylsulphanyl, C_{1-6}alkylsulphinyl, C_{1-6}alkylsulphonyl, sulphamoyl, *N*-(C_{1-6}alkyl)sulphamoyl and *N,N*-(C_{1-6}alkyl)$_2$sulphamoyl;

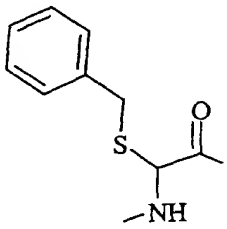
($\mathbf{AA^3}$) is selected from:



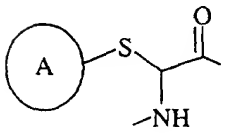
Phe(S),



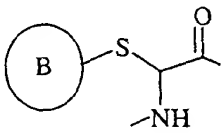
Leu(S),



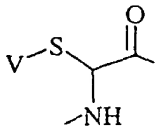
Phe(CH_2S),



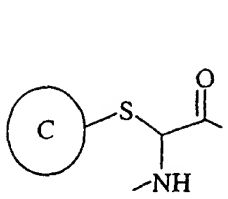
Cy(S)-Gly,



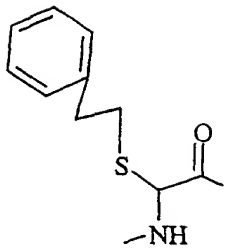
Hetar(S)-Gly,



alk(S)-Gly and



Het(S)-Gly, and



Phe(CH_2CH_2)S;

wherein Ring A is C_{3-12}cycloalkyl, Ring B is a 5 or 6 membered heteroaryl ring, Ring C is Het, V is C_{1-6}alkyl excluding isopropyl; the nitrogen of the amino acid may optionally be alkylated with C_{1-6}alkyl; the phenyl group of Phe(S) and Rings A and B may be optionally substituted with one or more of C_{1-6}alkyl, halo, trifluoromethyl, hydroxy, trifluoromethoxy, cyano, C_{1-6}alkoxy, C_{1-6}alkanoyl, C_{1-6}alkanoyloxy, amino, C_{1-6}alkylamino, *N,N*-(C_{1-6}alkyl)$_2$amino, C_{1-6}alkanoylamino, nitro, carboxy, carbamoyl, *N*-(C_{1-6}alkyl)carbamoyl, *N,N*-(C_{1-6}alkyl)$_2$carbamoyl, C_{1-6}alkoxycarbonyl, mercapto, C_{1-6}alkylsulphanyl, C_{1-6}alkylsulphinyl, C_{1-6}alkylsulphonyl, sulphamoyl, *N*-(C_{1-6}alkyl)sulphamoyl and *N,N*-(C_{1-6}alkyl)$_2$sulphamoyl; the phenyl group of Phe(S) may be fused to another phenyl group to form a naphthyl group; the sulphur moiety in the ∝-position of the amino acid (AA^3) may be optionally oxidised to form an -$S(O)_2$- or -S(O)- moiety; and

Het is a fully saturated monocyclic 5 - 8 membered heterocyclic ring, with up to 4 ring heteroatoms;

or a pharmaceutically acceptable salt thereof.

3. A compound as claimed in claim 2 wherein R^6 is hydrogen, optionally substituted phenyl or a 5 membered heteroaryl ring containing a maximum of four heteroatoms.

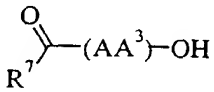
4. A compound as claimed in claim 2 or 3 wherein R^7 is benzyl (optionally substituted with halo (such as chloro)), α-(C_{1-4} alkyl)-benzyl (optionally substituted with halo (such as chloro)), α,α-di(C_{1-4} alkyl)-benzyl (optionally substituted with halo (such as chloro)), optionally substituted phenoxymethyl, phenylsulphonylmethyl, benzyloxy, naphthyl or optionally substituted phenyl where said optional substituents are chosen from one or more halo.

SUB 14

5. A compound as claimed in claim 2, 3 or 4 wherein (AA^3) is Leu(S), Phe(S) optionally substituted with C_{1-6}alkyl or halo and wherein the phenyl group of Phe(S) may be fused to another phenyl group to form a naphthyl group or the sulphur moiety in the ∝-position of the amino acid (AA) may be optionally oxidised to form an $-S(O)_2-$ or Phe(CH_2S).

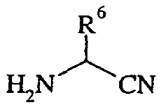
6. A process for preparing a compound of formula (Ia) as claimed in claim 2 comprising:

a) coupling an acid of formula **(IIIa)**:



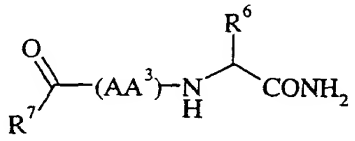
(IIIa)

or a reactive derivative thereof, with an amine of formula **(IVa)**:



(IVa)

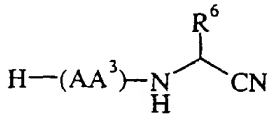
b) dehydrating a compound of formula **(Va)**:



(Va)

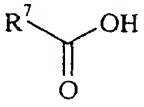
under standard conditions; or,

c) reacting an amine of formula **(VIa)**:



(VIa)

with an acid of formula **(VIIa)**:

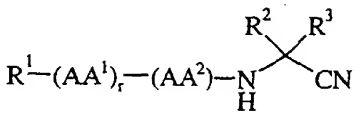


(VIIa)

or a reactive derivative thereof;

wherein R^6, R^7 and AA^3 are as defined in claim 2.

7. A compound of formula (I):



(I)

wherein:

r is 0 or 1;

R^1 is optionally substituted benzyl where said optional substituents are chosen from one or more of C_{1-6}alkyl, halo, trifluoromethyl, hydroxy, trifluoromethoxy, cyano, C_{1-6}alkoxy, C_{1-6}alkanoyl, C_{1-6}alkanoyloxy, amino, C_{1-6}alkylamino, *N,N*-(C_{1-6}alkyl)$_2$amino, C_{1-6}alkanoylamino, nitro, carboxy, carbamoyl, *N*-(C_{1-6}alkyl)carbamoyl, *N,N*-(C_{1-6}alkyl)$_2$carbamoyl, C_{1-6}alkoxycarbonyl, mercapto, C_{1-6}alkylsulphanyl, C_{1-6}alkylsulphinyl, C_{1-6}alkylsulphonyl, sulphamoyl, *N*-(C_{1-6}alkyl)sulphamoyl and *N,N*-(C_{1-6}alkyl)$_2$sulphamoyl or R^1 is a group of formula (II):

(II)

wherein R^5 is C_{1-6}alkyl (optionally substituted with an optionally substituted phenyl, an optionally substituted 5 or 6 membered heteroaryl ring, optionally substituted phenoxy or optionally substituted phenylsulphonyl), C_{1-6}alkoxy, optionally substituted phenyl, optionally substituted naphthyl, optionally substituted phenylC_{1-6}alkoxy where said optional substituents are chosen from one or more of C_{1-6}alkyl, halo, trifluoromethyl, hydroxy, trifluoromethoxy, cyano, C_{1-6}alkoxy, C_{1-6}alkanoyl, C_{1-6}alkanoyloxy, amino, C_{1-6}alkylamino, *N,N*-(C_{1-6}alkyl)$_2$amino, C_{1-6}alkanoylamino, nitro, carboxy, carbamoyl, *N*-(C_{1-6}alkyl)carbamoyl, *N,N*-(C_{1-6}alkyl)$_2$carbamoyl, C_{1-6}alkoxycarbonyl, mercapto, C_{1-6}alkylsulphanyl, C_{1-6}alkylsulphinyl,

C_{1-6}alkylsulphonyl, sulphamoyl, *N*-(C_{1-6}alkyl)sulphamoyl and *N,N*-(C_{1-6}alkyl)$_2$sulphamoyl;

R^2 is H, C_{1-6}alkyl [optionally substituted with one or more of hydroxy, C_{1-6}alkylsulphanyl, C_{1-6}alkylsulphinyl, C_{1-6}alkylsulphonyl, R^4, R^4C_{1-6}alkylsulphanyl, R^4C_{1-6}alkylsulphinyl, R^4C_{1-6}alkylsulphonyl], or R^2 is C_{1-6}alkoxy [optionally substituted with one or more of C_{2-6}alkenyl, C_{2-6}alkynyl, R^4, R^4C_{2-6}alkenyl, R^4C_{2-6}alkynyl, Het and trifluoromethyl], or R^2 is C_{2-6}alkenyl, C_{2-6}alkynyl, C_{1-6}alkoxycarbonyl, carbamoyl, *N*-(C_{1-6}alkyl)carbamoyl, *N,N*-(C_{1-6}alkyl)$_2$carbamoyl, R^4, R^4S, R^4C_{1-6}alkylsulphanyl, *N*-(R^4C_{1-6}alkyl)carbamoyl, *N*-(HetC_{1-6}alkyl)carbamoyl, C_{1-6}alkanoylamino, C_{1-6}alkylsulphanyl, C_{1-6}alkylsulphinyl, C_{1-6}alkylsulphonyl wherein **R^4** is an optionally substituted phenyl, or an optionally substituted 5 or 6 membered heteroaryl ring containing a maximum of four heteroatoms said optional substituents being chosen from one or more of C_{1-6}alkyl, halo, trifluoromethyl, hydroxy, trifluoromethoxy, cyano, C_{1-6}alkoxy, C_{1-6}alkanoyl, C_{1-6}alkanoyloxy, amino, C_{1-6}alkylamino, *N,N*-(C_{1-6}alkyl)$_2$amino, C_{1-6}alkanoylamino, nitro, carboxy, carbamoyl, *N*-(C_{1-6}alkyl)carbamoyl, *N,N*-(C_{1-6}alkyl)$_2$carbamoyl, C_{1-6}alkoxycarbonyl, mercapto, C_{1-6}alkylsulphanyl, C_{1-6}alkylsulphinyl, C_{1-6}alkylsulphonyl, sulphamoyl, *N*-(C_{1-6}alkyl)sulphamoyl and *N,N*-(C_{1-6}alkyl)$_2$sulphamoyl;

R^3 is H or C_{1-6}alkyl; and

(**AA^1**) and (**AA^2**) are independently chosen from Ala, Arg, Cys, Gly, His, Ile, Leu, Lys, Met, Phe, Ser, Thr, Trp, Tyr, Val, Lys(CHO), Arg(NO_2), β-Ala, Ser(Bzl), Ph-Gly, Nle, Ser(O^{t}Bu), His(Bzl), Met(O), Cha, His(Me), Cit, Tyr(^{t}Bu), Met(O_2), Pyr-Ala, Phe(S), Leu(S) or Phe(CH_2S); wherein the nitrogen of the amino acid may optionally be alkylated with C_{1-6}alkyl and the phenyl group of Phe(S) may be optionally substituted with one or more of C_{1-6}alkyl, halo, trifluoromethyl, hydroxy, trifluoromethoxy, cyano, C_{1-6}alkoxy, C_{1-6}alkanoyl, C_{1-6}alkanoyloxy, amino, C_{1-6}alkylamino, *N,N*-(C_{1-6}alkyl)$_2$amino, C_{1-6}alkanoylamino, nitro, carboxy, carbamoyl, *N*-(C_{1-6}alkyl)carbamoyl, *N,N*-(C_{1-6}alkyl)$_2$carbamoyl, C_{1-6}alkoxycarbonyl, mercapto, C_{1-6}alkylsulphanyl, C_{1-6}alkylsulphinyl, C_{1-6}alkylsulphonyl, sulphamoyl, *N*-(C_{1-6}alkyl)sulphamoyl and *N,N*-(C_{1-6}alkyl)$_2$sulphamoyl or the phenyl group may be fused to another phenyl group to form a naphthyl group; or a pharmaceutically acceptable salt thereof.

8. A compound of formula (I) as claimed in claim 7 wherein r is 0; and R^2 is furyl, pyrazolyl (optionally substituted with one or more of methyl and bromo), imidazolyl, 1,2,4-triazolyl, benzyl, 2-methylthioethyl, isopropylthio, methoxy, isopropoxy and 2-propynyloxy.

9. A compound of formula (I) as claimed in claim 1 wherein r is 0; and R^2 is thienyl.

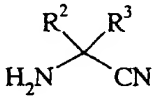
10. A process for preparing a compound of formula (I) as claimed in claim 1 comprising:

a) coupling an acid of formula (**III**):

$$R^1-(AA^1)_r-(AA^2)-OH$$

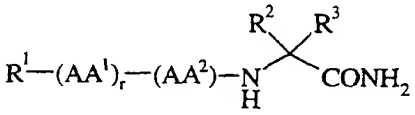
(**III**)

or a reactive derivative thereof, with an amine of formula (**IV**):



(**IV**)

b) dehydrating a compound of formula (**V**):



(**V**)

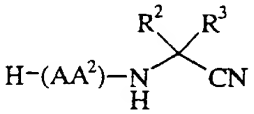
under standard conditions;

c) for compounds of formula (**I**) where r = 1, coupling an acid of formula (**VI**):

$$R^1-(AA^1)-OH$$

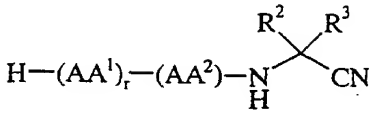
(**VI**)

or a reactive derivative thereof as defined hereinbefore, with an amine of formula (**VII**):



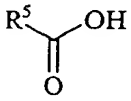
(**VII**)

d) for compounds of formula (I) where R^1 is a group of formula (II), reacting an amine of formula (VIII):



(VIII)

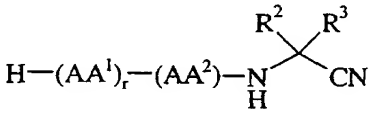
with an acid of formula (IX):



(IX)

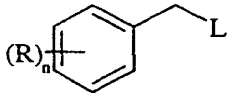
or a reactive derivative thereof as defined hereinbefore; or

e) for compounds of formula (I) where R^1 is optionally substituted benzyl, reacting an amine of formula (X):



(X)

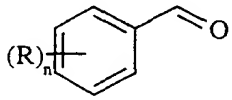
i) with a compound of formula (XI):



(XI)

where $(R)_n$ are optional substituents as defined above and L is a displaceable group; or

ii) with an aldehyde of formula (XII):

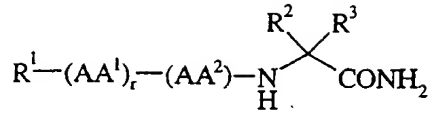


(XII)

where $(R)_n$ are optional substituents as defined above and L is a displaceable group;

wherein R^1, R^2, R^3, AA^1, AA^2 and r are as defined in claim 1.

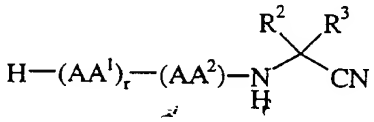
11. A compound of formula (V):



(V)

wherein R^1, R^2, R^3, AA^1, AA^2 and r are as defined in claim 1.

12. A compound of formula (VIII):



(VIII)

wherein R^1, R^2, R^3, AA^1, AA^2 and r are as defined in claim 1.

13. A pharmaceutical composition comprising a compound of formula (I) or (Ia), or a pharmaceutically acceptable salt thereof, as claimed in claim 1, 2, 8 or 9 and a pharmaceutically acceptable diluent or carrier.

14. A compound of formula (I) or (Ia), or a pharmaceutically acceptable salt thereof, as claimed in claim 1, 2, 8 or 9 for use as a medicament

15. The use of a compound of formula (I) or (Ia) as claimed in claim 1, 2, 8 or 9, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for use in the inhibition of a cysteine protease in a warm blooded animal.

16. The use of a compound of formula (I) or (Ia) as claimed in claim 1, 2, 8 or 9, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for use in the treatment of chronic obstructive pulmonary disease in a warm blooded animal.

17. A method of treating a Cathepsin L or Cathepsin S mediated disease state in mammals which comprises administering to a mammal in need of such treatment an effective

amount of a compound of formula (I) or (Ia) as claimed in claim 1, 2, 8 or 9, or a pharmaceutically acceptable salt thereof.